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Prevalence of Hepatitis B and C in US Air Force Basic Military Trainees from Blood Donations 1 2 Douglas F. Taylor, DO (Capt, USAF)1; Maj. Ryan S. Cho, MD (Maf, USAF)1; Lt Col Jason F. Okulicz, 3 MD (Lt Col, USAF)2; Maj Bryant J. Webber, MD, MPH (Maj, USAF)3; Lt Col John G. Gancayco, MD 4 $(Maj, USAF)^{1}$ 5 6 Abstract Hepatitis B virus (HBV) and hepatitis C virus (HCV) can cause significant morbidity in military service 7 members and may potentially negatively impact mission readiness. Prevalence among military recruits 8 accessioning into the United States Air Force for hepatitis B and C has not previously been described. 9 The Joint Base San Antonio-Lackland Blood Donor Center was queried for HBV and HCV screening for 10 all basic military trainees who donated blood between November 25, 2013 through April 16, 2016. Other 11 populations, such as active duty or reserve personnel, were excluded. The estimated prevalence of HBV 12 and HCV was 0.0098% and 0.007%, respectively. This study suggests that the overall estimated 13 prevalence of HBV and HCV infection is much lower among USAF basic trainees compared to both the 14 active duty and US civilian populations. HBV and HCV are viral infections that can negatively impact 15 mission readiness, individual deployment status, and have significant costs for the military. Additional 16 studies are needed to determine cost effectiveness of screening for viral hepatitis among military 17 18 populations. Disclaimer: The opinions expressed by the authors contributing to this manuscript do not necessarily 19 reflect the opinions of the Department of Defense or the institutions with which the authors are affiliated. 20 21 Introduction Chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) infections can cause significant 22 morbidity in military service members due to prolonged inflammatory damage to the liver and potential 23 complications including cirrhosis, hepatocellular carcinoma, and fulminant liver failure which would may 24 necessitate liver transplantation. 1,2 The estimated prevalence of chronic hepatitis B infection in the 25 United States civilian population is 0.4%, however it is possible that the prevalence in the civilian 26

population is underestimated as prior studies assessing hepatitis B prevalence in the civilian population excluded groups of people at higher risk of infection such as Asians, Pacific Islanders, and homeless populations³. The overall prevalence of chronic hepatitis C in the United States has been found to be 0.48%, 5.4% and 1.6% for active duty, veteran, and civilian populations respectively. ^{4,5,6} The prevalence of chronic hepatitis B infections among residents of group quarters, such as military barracks, college dormitories, nursing homes, and long-term care facilities in the United States has been estimated as approximately 0.5%.⁹

Although the overall prevalence and incidence rates of chronic HBV and HCV are well known in the active duty population, prevalence among military recruits accessioning into the United States Air Force has not been described. Incoming trainees are not routinely screened for acute or chronic hepatitis B and C infection. They are screened for immunity for hepatitis B, and given the vaccination series if negative for the hepatitis B surface antibody. Screening for hepatitis B immunity involves screening only for the surface antibody alone, with a positive test indicating immunity from prior vaccination.

Interpretation of serology for Acute and chronic hepatitis B infections, along with the different phases of chronic infection are summarized in table 2. Identifying the prevalence of acute and chronic HBV and HCV is important not only due to the possible health consequences of these infections, but also due to the high cost of clinical evaluation and treatment. Identifying recruits with acute and chronic HBV or HCV is likely beneficial to the military from a mission readiness standpoint as these individuals do not meet the standards for entry into active military service and disease management costs would be shifted to the civilian sector.

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Methods

The Joint Base San Antonio-Lackland Blood Donor Center was queried for the results of HBV and HCV screening for all basic military trainees who donated blood between November 25, 2013 through April 16, 2016. A total of 30,660 basic trainees donated blood. Other populations, such as active duty or reserve personnel, were excluded. Demographic data included age, race, sex, and state or country of origin.

Blood from trainees donors was screened for the presence of HBV surface antigen and HCV antibody. If the donated blood was positive for HBV surface antigen, the confirmatory testing was for HBV core antibody and HBV DNA. If positive for HCV antibody, the confirmatory testing was for HCV RNA. Estimated HBV and HCV prevalence among basic trainees who donated blood were calculated with the 30,660 trainees that donated blood used as the denominator to determine prevalence. This retrospective study was approved by the Wilford Hall IRB.

Results

An estimated 30,660 basic trainees donated blood during the study period with approximately 140 basic trainees donating blood each week. A total of 44 basic trainees who donated blood had a positive screen for either HBV or HCV infection during the study period. Five of the trainee donors were positive for HBV surface antigen, and three of them subsequently tested positive for HBV core antibody and HBV DNA. Of the 39 trainee donors who tested positive for HCV antibody, two subsequently tested positive for HCV RNA. Cases were predominantly male (1 female with HCV) and the age range was 18-33 years.

The 3 trainees with confirmed HBV infection were of Asian descent, with 2 from being born in Hawaii and 1 born in Vietnam. The 2 trainees with confirmed HCV infection were both white and were born in Missouri and California (table 1). Based on the estimated number of basic trainees who donated blood during the study period, the estimated prevalence of HBV and HCV was 0.0098% and 0.007% respectively.

Discussion

This study suggests that the overall estimated prevalence of HBV and HCV infection is much lower among USAF basic trainees compared to both the active duty and US civilian populations. This may be secondary to a reduction in risk factors for HBV and/or HCV as most of the trainees that donated bloodlikely did not have blood transfusions prior to 1992 (many were born after 1992), were not born during high risk time interval, and presumably lack other risk factors that would increase the risk of acquisition such as high risk sexual behaviors or intravenous drug use. ⁷

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The prior studies in active duty and civilian populations showed a higher prevalence of HCV among non-hispanic blacks and other racial/ethnic groups. ⁸ This study in contrast revealed HCV was confined to whites. The small number of cases presented in this study limits the significance of this finding and the ability to make comparisons. ⁹ Of the patients that were positive for HBV, all were of Asian or Pacific Islander descent which is consistent with the higher prevalence noted in civilian Asian and Pacific Islanders in the United States. ¹⁰

Screening for HBV immunity occurs at the start of basic training. However HBV screening for immunity involves only screening for the HBV surface antibody, and does not include screening other markers that suggest acute or chronic infection such as the HBV core antibody, HBV e-antgien, HBV e-antidboy, and HBV DNA. Some patients could potentially harbor HBV in an inactive carrier state and if the virus becomes active then the risk of cirrhosis and hepatocellular carcinoma (HCC) are higher than HCV. Screening for HBV includes HBV surface antigen, costing \$99 per person and not cost effective due to very low prevalence in our population. However, it may be reasonable to consider targeting testing of populations that are at higher risk for HBV such as foreign born Asian and Pacific Islanders.

The prior study by Brett-Major et al evaluating the active duty population with assumptions suggested a cost benefit to HCV screening. Although the cost of HCV treatment varies based on viral genotype, most new drug regimens targeted at genotype 1 cost approximately \$100,000. Assuming a screen of the estimated 30,660 basic trainees who donated blood during this study period would cost

\$10.84 per test, a total of \$332,354 would be spent on screening alone, with an additional small cost added for confirmatory testing, compared to approximately \$200,000 spent to treat the 2 positive cases of HCV ¹¹. It is likely that if the total number of recruits were screened rather than only those that donated blood, that there would be more positive tests for HBV and HCV infection, with the costs of screening potentially exceeding the cost of treatment. Based on this data, this study demonstrates no cost benefit to accession screening for HCV, in comparison to providing treatment of those who are HCV-infected and otherwise have been prevented from entering military service. This discrepancy in the cost-benefit analysis is attributed to the difference in the lower prevalence demonstrated in this study of 0.007% (versus 0.043%, Brett-Major et al), leading to the higher cost of screening weighed against the lower cost of treatment. This analysis however does not factor in the potential long-term costs to the U.S. medical system of managing patients with liver complications due to HCV such as HCC and/or cirrhosis, due to delay diagnosis and treatment.

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The limitation of the study includes the sample size and the study population chosen for the study, only including the basic trainees donating blood. This fails to capture the infected basic trainees who chose not to donate blood, leading to possible selection bias due to the healthy donor effect. Donors when compared to the general population tend to be younger, healthier, and likely exposed to less risk factors for acquisition of viral hepatitis, which may potentially the lower prevalence rate of HCV and HBV infection within our study population. However, given our n of 30,660, and the relative health and youth of young military recruits in general, this is unlikely to drastically have changed the results of our study.

HBV and HCV are viral infections that can negatively impact mission readiness, individual deployment status, and have significant costs for the military. Accession screening for HCV does not appear to offer a cost-benefit given the lower costs associated with treatment disease, while a discussion in regards to screening for populations at risk for hepatitis B may be more reasonable, given the much

higher costs associated with screening for HBV. Additional studies are needed to determine cost 124 effectiveness of screening for viral hepatitis among military populations. 125 Author affiliations: Gastroenterology Service, San Antonio Military Medical Center, 3551 Roger Brooke Drive, 126 Fort Sam Houston TX 78234; ²Infectious Disease Service, San Antonio Military Medical Center, 3551 Roger Brooke 127 Drive, Fort Sam Houston TX 78234; 3 Preventative Medicine Joint Base San Antonio Lackland, 2200 Bergquist Dr, 128 San Antonio, TX 78236. 129 130 Funding: None to report. 131 132 133 134 References 135 1. Hiotis SP, Rahbari NN, Villanueva GA, et al: Hepatitis B vs. Hepatitis C Infection on Viral Hepatitis-136 Associated Hepatocellular Carcinoma. BMC Gastroenterol. 2012;12(64) 13.7 138 2. Armed Forces Health Surveillance Center AFHSC: Viral hepatitis C, active component, US Armed 139 Forces, 2000-2010. MSMR 2011; 18(8), p.10. 140 141 3. Kim WR: Epidemiology of Hepatitis B in the United States. Hepatology 2009; 49(5 suppl): S28-S34 142 143 4. Armstrong GL, Wasley A., Simard EP, et al: The prevalence of hepatitis C virus infection in the 144 United States, 1999 through 2002. Annals of internal medicine 2006; 144(10), pp.705-714. 145 146 5. Phillips FH and Barnes DM: Meaning of Adherence in Hepatitis C-Infected Military Veterans. 147 Gastroenterology Nursing 2016; 39(1), pp.17-23. 148 149

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Table 1. Basic Trainees with positive testing to hepatitis C and hepatitis B

| Characteristics | HCV+ | HBV+ | |
|------------------|------|------|---|
| Sex | | | |
| -Male | | 1 | 3 |
| -Female | | 1 | 0 |
| Race | | | |
| -White | | 2 | 0 |
| -African America | an | 0 | 0 |
| -Asian | | 0 | 3 |
| -Other | | 0 | 0 |

Table 2. Hepatitis B serologic testing

| HBV surface antigen | HBV IgM core |
|---------------------|--------------|
| X | X |
| | |
| | |
| | |
| X | |
| x | |
| X | x |
| | x x x |

| HBV lgG core | HBV lgG core HBV e-antigen | HBV e-antibody | HBV e-antibody HBV surface antibody | HBV DNA |
|--------------|----------------------------|----------------|-------------------------------------|---------|
| × | × | | | >20,000 |
| × | | × | × | |
| | | | × | |
| × | * | | | >20,000 |
| × | | × | | -/+ |
| × | -/+ | | | >2000 |